RHÔNE-POULENC

TOXICOLOGY DEPARTMENT
P.O. BOX 12014, 2 T.W. ALEXANDER DRIVE
RESEARCH TRIANGLE PARK, NC 27709
(919) 549-2000 TELEFAX (919) 549-8525
INTERNATIONAL TELEX NUMBER 4999378-ANSWERBACK APC RTP

Contains NO CBI

92 OCT 13 AM 8:18

October 5, 1992

A

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

8EHQ-92-12597

8892000107 81

INIT

Document Processing Center (TS-790)
Office of Toxic Substances
US Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

Attn: Section 8(e) Coordinator (CAP Agreement)

RE: Report Submitted Pursuant to the TSCA Section 8(e) Compliance Audit Program

CAP ID No.: 8ECAP - 0004

Dear Sir/Madam:

On behalf of Rhône-Poulenc Inc. (RPI, CN 5266, Princeton, NJ 08543-5266) and its subsidiary Rhône-Poulenc Ag Company, the attached study report is being submitted to the Environmental Protection Agency (EPA) pursuant to the Toxic Substances Control Act (TSCA) Section 8(e) Compliance Audit Program and the Agreement for a TSCA Section 8(e) Compliance Audit Program (CAP Agreement) executed by RPI and EPA.

The enclosed study report provides information on MCA 600. The CAS number and name for this chemical are 1079-33-0 and benzo[b]thiophene-4-ol, methylcarbamate. This chemical was synthesized for pesticide research and development approximately 20 to 25 years ago. To our knowledge, a pesticide application on this chemical has never been submitted to EPA under the Federal Insecticide, Fungicide, and Rodenticide Act.

No claims of confidentiality are made for this submission. The title of the enclosed report is "MCA-600 (50% Wettable Powder) Safety Evaluation By: Acute Inhalation Exposure to Rats and Acute Dermal Application to Rabbits". The following is a summary of the adverse effects observed in this study.

This study is being submitted under Section 8(e) because of clinical signs observed during the inhalation study. Groups of 5 male and 5 female rats were exposed to gravimetric concentrations of either 0.95, 5.7, or 8.2 mg/L for one hour. Signs of toxicity consisted of tremors, ataxia, exophthalmos, and excessive salivation. The onset of these signs occurred within 30 minutes after initiation of exposure and persisted for 9 days in the 8.2 mg/L group and for 2 days at the lower levels. The one-hour LC50 was calculated to be 5.7 mg/L. In the dermal study, no systemic toxicity was observed at dose levels up to 2000 mg/kg.

No previous TSCA Section 8(e) notices have been submitted on this chemical, but a total of three submissions will be made under the CAP.

3/15/95

In total, RPI is submitting three copies of the enclosed report and this cover letter: an original and two copies.

Further questions regarding this submission may be directed to the undersigned at 919-549-2222.

Sincerely,

Glenn S. Simon, PhD, DABT
Director of Toxicology

Copy for: W. W. Phillips

TELEPHONE: 437-1600

WOODARD RESEARCH CORPORATION

LABORATORY AND CONSULTING SERVICE

P. O. BOX 405, HERNDON, VIRGINIA 22070

December 13, 1965

Dr. J. R. Kilsheimer
Manager, Organic Chemicals
Research and Technical Division
Mobil Chemical Company
Metuchen, New Jersey 08840

Dear Doctor Kilsheimer:

Enclosed are 10 copies of a report dealing with the safety evaluation of MCA-600 (50% Wettable Powder) by inhalation exposure in rats and dermal application in rabbits. I believe that the report is self-explanatory. However, if there are any questions or comments, please do not hesitate to let us know.

In your letter dated August 26, 1965, you indicate that an emulsifiable concentrate will be sent to us for testing. As of this date we have not received that material.

Sincerely yours,

Robert P. Beliles, Ph.D.
Pharmacologist

RPB:jee

Enclosures

WOODARD RESEARCH CORPORATION

MOBIL CHEMICAL COMPANY

MCA-600 (50% WETTABLE POWDER)

SAFETY EVALUATION BY:

ACUTE INHALATION EXPOSURE TO RATS

ACUTE DERMAL APPLICATION TO RABBITS

MATERIAL TESTED: A cream colored powder labeled:

EXPERIMENTAL INSECTICIDE
MCA-600 (Ent. 27041)
50% Wettable Powder

was received from Mobil Chemical Company on August 24, 1965, and used in the studies described herein.

ACUTE INHALATION EXPOSURE TO RATS

PROCEDURE: Thirty rats from The Charles River Breeding Laboratories were acclimated to our laboratory environment for at least one week and then exposed for one hour to an aerosol as follows:

Group	Number per Group	Chamber Concentration MCA-600 (50% Wettable Powdc mg/l
I	5 males, 5 females	8.2
II	5 males, 5 females	5.7
III	5 males, 5 females	0.95

The exposure chamber was 30 liters in capacity and similar to that described by Leach (University of Rochester, Atomic Energy Project Report, UR-629, 1963).

The chamber concentrations were determined gravimetrically, using a 2-inch glass fiber filter (Gelman Type A). By use of UNICO model 2.8 Respirable Dust Sampler, it was estimated that 9 per cent of the aerosol was of aerodynamic size to be considered respirable in man.

Immediately after exposure excess material was removed from the coat, nostrils, and eyes of the experimental animals. The rats were then maintained for 14 days in individual cages and provided food and water ad libitum. Body weights were obtained prior to exposure and at 7 and 14 days. The animals were observed closely during exposure and daily thereafter for signs of toxicity.

The animals which died during exposure or before the fourteenth day were examined for gross changes. The surviving animals were sacrificed, examined for gross changes and the lungs, heart, liver, kidney, and brain weighed.

RESULTS: The mortality 14 days after exposure was as follows:

Chamber Concentration MCA-600 (50% Wettable Powder) mg/l	Mortality
8.2	6/10
5.7	5/10
0.95	0/10

All deaths occurred during exposure or within 24-hours afterward. No marked difference in susceptibility between males and females was noted. An LC_{50} for MCA-600 (50% wettable powder) of 5.7 mg/l with 95 per cent confidence limits of 1.34-16.4 was obtained by the method of Litchfield and Wilcoxon.

Signs of toxicity consisted of tremors, ataxia, exophthalmos, and excessive salivation. The onset of these signs occurred within 30 minutes after the start of the exposure and lasted for nine days in the animal exposed at a level of 8.2 mg/l and for two days at the lower levels. The body weights in Groups I and II of most animals taken at the seventh day were lower than the initial weights. All animals gained weight between the seventh and fourteenth day.

Necropsy findings consisted of scattered lung hemorrhage in all groups, enlarged right kidney (rat No. 4490 F - 0.95 mg/l), and pale kidneys (rat No. 4545 M - 5.7 mg/l).

CONCLUSIONS: On the basis of one hour inhalation exposures of MCA-600 (50% Wettable Powder) at levels of 8.2 mg/l, 5.7 mg/l and 0.95 mg/l in rats, it is concluded that:

The LC_{50} (1 hour exposure) for MCA-600 (50% wettable powder) is 5.7 mg/l (1.34-16.4).

ACUTE DERMAL APPLICATION TO RABBITS

PROCEDURE: Three groups consisting of four adult albino rabbits each were prepared for study by closely clipping the fur on the back and trunk of all animals. Individual rabbit weights ranged between 2.2 and 2.8 kilograms; the rabbits had been acclimated to local conditions for at least one week before the experiment began.

The respective doses of MCA-600 (50% wettable powder) were placed on gauze, moistened with saline, and applied to the backs of the rabbits. Then each animal was wrapped with rubber damming which was fastened in place, and returned to its cage where food and water were readily available. The doses used were 2000, 632, and 200 mg/kg of MCA-600 (50% wettable powder).

After 24 hours the wrappings were removed, residual test material was wiped off and the rabbits were examined for signs of skin irritation and systemic toxicity.

Daily examinations of each rabbit were made for seven days. After this time the rabbits were sacrificed and autopsied.

RESULTS: Data are appended for each rabbit. Skin irritation was confined largely to a slight erythema observed only on the first experimental day. Two rabbits (No. 6458 M - 2000 mg/kg and No. 6472 F - 200 mg/kg) had soft feces for several days after treatment.

Autopsy of the rabbits showed scattered evidence of lung hemorrhage, kidney discoloration, pitted kidneys, and accumulation of peritoneal fluid. These findings, because of lack of dose relationship, were felt to be of doubtful significance.

It is concluded that MCA-600 (50% wettable powder) is a very mild irritant at a single dose of 632 mg/kg or more, but that 200 mg/kg produces no effects on the skin. Furthermore, no systemic toxicity is produced by a single dermal application of 2000 mg/kg of MCA-600 (50% wettable powder).

Robert P. Beliles, Ph.D.
Pharmacologist

December 13, 1965

Clara Kidwell, B.S.
Analyst

MCA-600

WEEKLY BODY WEIGHTS IN GRAMS FOR MALE RATS

Rat No. and Sex	Days 0	7	14
	LEVEL - 8.2 MG/L		
4563 M	319	305	349
4564 M	331	330	371
4565 M	319	Dead	
4566 M	292	Dead	
4567 M	264	Dead	
Mean	305	315	355
	LEVEL - 5.7 MG/L		
4543 M	279	275	310
4544 M	282	249	290
4545 M	270	279	318
4546 M	320	Dead	
4547 M	292	Dead	
Mean	289	268	306
	LEVEL - 0.95 MG/L		
4483 M	388	406	431
4484 M	486	501	516
4485 M	462	466	498
4486 M	421	443	478
4487 M	458	481	515
Mean	443	459	488

MCA-600

WEEKLY BODY WEIGHTS IN GRAMS FOR FEMALE RATS

Rat No. and Sex	Days 0	7	14
	LEVEL - 8.2 MG/L		
4568 F	261	226	243
4569 F	250	228	252
4570 F	244	Dead	
4571 F	224	Dead	
4572 F	218	Dead	
Mean	239	227	248
	LEVEL - 5.7 MG/L		
4548 F	203	181	198
4549 F	226	Dead	
4550 F	213	208	232
4551 F	213	Dead	
4552 F	222	Dead	
Mean	215	195	215
	LEVEL - 0.95 MG/L		
4488 F	269	259	276
4489 F	245	259	272
4490 F	262	253	263
4491 F	253	250	266
4492 F	242	248	263
Mean	254	254	268

MCA-600

RELATIVE ORGAN WEIGHTS IN GRAMS FOR MALE RATS

Rat No. and Sex	Body Weight g	Liver g	Lung g	Kidney g	Brain g	Heart g
			LEVEL - 8.2 MG/L			
4563 M	349	4.16	0.659	0.885	0.559	0.347
4564 M	371	3.68	0.480	0.862	0.534	0.299
Mean	360	3.79	0.570	0.874	0.547	0.323
			LEVEL - 5.7 MG/L			
4543 M	310	3.43	0.710	0.829	0.600	0.339
4544 M	290	4.32	0.738	0.910	0.659	0.321
4545 M	318	3.78	0.648	0.884	0.579	0.327
Mean	306	3.84	0.699	0.874	0.613	0.329
			LEVEL - 0.95 MG/L			
4483 M	431	3.43	0.392	0.548	0.476	0.269
4484 M	516	3.22	0.760	0.678	0.428	0.308
4485 M	498	3.78	0.478	0.673	0.432	0.289
4486 M	478	3.34	0.785	0.684	0.400	0.297
4487 M	515	3.88	0.486	0.761	0.383	0.266
Mean	488	3.53	0.580	0.669	0.424	0.286

MCA-600

RELATIVE ORGAN WEIGHTS IN GRAMS FOR FEMALE RATS

Rat No. and Sex	Body Weight g	Liver g	Lung g	Kidney g	Brain g	Heart g
			LEVEL - 8.2 MG/L			
4568 F	243	3.73	0.864	0.802	0.679	0.354
4569 F	252	3.98	0.802	0.861	0.718	0.385
Mean	248	3.86	0.833	0.832	0.699	0.370
			LEVEL - 5.7 MG/L			
4548 F	198	3.64	0.667	0.813	0.914	0.399
4550 F	232	3.16	2.20	0.836	0.784	0.366
Mean	215	3.40	1.43	0.825	0.849	0.383
			LEVEL - 0.95 MG/L			
4488 F	276	3.21	0.630	0.696	0.667	0.391
4489 F	272	3.35	0.610	0.676	0.757	0.320
4490 F	263	3.24	0.517	1.06	0.719	0.373
4491 F	266	3.10	0.846	0.669	0.684	0.308
4492 F	263	3.58	0.707	0.787	0.757	0.342
Mean	268	3.30	0.662	0.778	0.717	0.347

MCA-600

ABSOLUTE ORGAN WEIGHTS IN GRAMS FOR MALE RATS

Rat No. and Sex	Body Weight	Liver	Lungs	Kidneys	Brain	Heart
	g	g	g	g	g	g
			LEVEL - 8.2 MG/L			
4563 M	349	14.5	2.30	3.09	1.95	1.21
4564 M	371	13.7	1.78	3.20	1.98	1.11
Mean	360	14.1	2.04	3.11	1.97	1.16
			LEVEL - 5.7 MG/L			
4543 M	310	10.6	2.20	2.57	1.86	1.05
4544 M	290	12.5	2.14	2.64	1.91	0.93
4545 M	318	12.0	2.06	2.81	1.84	1.04
Mean	306	11.7	2.13	2.67	1.87	1.01
			LEVEL - 0.95 MG/L			
4483 M	431	14.8	1.69	2.36	2.05	1.16
4484 M	516	16.6	3.92	3.50	2.21	1.59
4485 M	498	18.8	2.38	3.35	2.15	1.44
4486 M	478	15.9	3.75	3.27	1.91	1.42
4487 M	515	20.0	2.50	3.92	1.97	1.37
Mean	488	17.2	2.85	3.28	2.06	1.40

MCA-600

ABSOLUTE ORGAN WEIGHTS IN GRAMS FOR FEMALE RATS

Rat No. and Sex	Body Weight g	Liver g	Lungs g	Kidneys g	Brain g	Heart g
			LEVEL - 8.2 MG/L			
4568 F	243	9.1	2.10	1.95	1.65	0.86
4569 F	252	10.0	2.02	2.17	1.81	0.97
Mean	248	9.55	2.06	2.06	1.73	0.915
			LEVEL - 5.7 MG/L			
4548 F	198	7.21	1.32	1.61	1.81	0.79
4550 F	232	7.34	5.11	1.94	1.82	0.85
Mean	215	7.28	3.22	1.78	1.83	0.82
			LEVEL - 0.95 MG/L			
4488 F	276	8.86	1.74	1.92	1.84	1.08
4489 F	272	9.12	1.66	1.84	2.06	0.87
4490 F	263	8.52	1.36	2.79	1.89	0.98
4491 F	266	8.25	2.25	1.78	1.82	0.82
4492 F	263	9.41	1.86	2.07	1.99	0.90
Mean	268	8.83	1.77	2.08	1.92	0.93

MCA-600

ACUTE DERMAL TOXICITY FOR THE RABBIT

Rabbit No. and Sex	Dose mg/kg	Body Weight (kg) Initial	Body Weight (kg) Sacrifice	Days 1	2	3	4	5	6	7
No. 6458 M	2000	2.58	2.61							
Edema				-	-	-	-	-	-	-
Erythema				+	-	-	-	-	-	-
				Clear fluid in peritoneal cavity						
No. 6533 M	2000	2.54	2.61							
Edema				+	-	-	-	-	-	-
Erythema				+	-	-	-	-	-	-
				Lungs appeared hemorrhagic						
No. 6502 F	2000	2.45	2.50							
Edema				-	-	-	-	-	-	-
Erythema				-	-	-	-	-	-	-
				No apparent abnormalities						
No. 6468 F	2000	2.85	2.79							
Edema				-	-	-	-	-	-	-
Erythema				+	-	-	-	-	-	-
				Lungs appeared hemorrhagic						

MCA-600

ACUTE DERMAL TOXICITY FOR THE RABBIT

Rabbit No. and Sex	Dose mg/kg	Body Weight (kg) Initial	Body Weight (kg) Sacrifice	Days 1	2	3	4	5	6	7
No. 6534 M	632	2.37	2.50							
Edema				-	-	-	-	-	-	-
Erythema				-	-	-	-	-	-	-
				No abnormalities						
No. 6460 M	632	2.50	2.55							
Edema				-	-	-	-	-	-	-
Erythema				-	-	-	-	-	-	-
				Liver appeared to have parasites						
No. 6469 F	632	2.50	2.48							
Edema				-	-	-	-	-	-	-
Erythema				+	-	-	-	-	-	-
				Liver appeared to have parasites						
No. 6470 F	632	2.78	2.70							
Edema				-	-	-	-	-	-	-
Erythema				-	-	-	-	-	-	-
				Kidneys discolored - lungs slightly hemorrhagic						

MCA-600

ACUTE DERMAL TOXICITY FOR THE RABBIT

Rabbit No. and Sex	Dose mg/kg	Body Weight (kg) Initial	Body Weight (kg) Sacrifice	Days 1	2	3	4	5	6	7
No.6461 M	200	2.75	2.89							
Edema				-	-	-	-	-	-	-
Erythema				-	-	-	-	-	-	-
				No gross abnormalities apparent						
No. 6462 M	200	2.78	2.81							
Edema				-	-	-	-	-	-	-
Erythema				-	-	-	-	-	-	-
				No gross abnormalities apparent						
No. 6471 F	200	2.18	2.15							
Edema				-	-	-	-	-	-	-
Erythema				-	-	-	-	-	-	-
				Kidneys pitted - no other abnormalities						
No. 6472 F	200	2.74	2.90							
Edema				-	-	-	-	-	-	-
Erythema				-	-	-	-	-	-	-
				Kidneys pitted - no other abnormalities						

Triage of 8(e) Submissions

Date sent to triage: 2/5/96

NON-CAP CAP

Submission number: 12597 A

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX CTOX EPI RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

For Contractor Use Only

entire document: 0 1 2 **pages** 1,2 **pages** 1,2, tabs

Notes:

Contractor reviewer : LPS **Date:** 5/11/95

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ-1092-12597 SEQ. A

TYPE: (INT) SUPP FLWP

SUBMITTER NAME: Rhone-Poulenc Inc.

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0638) REFER TO CHEMICAL SCREENING
(0678) CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKER PROTECTION
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 10/05/92 OTS DATE: 10/13/92 CSRAD DATE: 03/15/95

CHEMICAL NAME:
Benzo[b]thiophene-4-ol, methylcarbamate
MCA 600

CASE
1079-33-0
II

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
(0209)	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
(0212)	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
(0243)	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
(0248)	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

TRIAGE DATE:

NON-CBI INVENTORY:
YES
CAS SR
NO
(IN TRIAGE)

ONGOING REVIEW:
YES (DROP/REFER)
NO (CONTINUE)
REFER

SPECI:
RAT
RBT

TOXICOLOGICAL CONCERN:
(LOW) Acute Inhalation Toxicity, Acute Dermal Toxicity, Dermal Irritation
MED
HIGH

USE: [redacted]
R&D Insecticide

PRODUCTION:

COMMENTS:

#12597A
L

Acute inhalation toxicity is of low concern based on a calculated 1-hour LC50 of 5.7 g/m^3 in rats. Mortality and corresponding doses (g/m^3) were 0/10 (0.95), 5/10 (5.7) and 6/10 (8.2). Clinical signs included tremors and ataxia (all doses), and necropsy findings included lung hemorrhage (all doses), pale kidneys (5.7) and enlarged kidney (0.95).

L

Acute dermal toxicity is of low concern based on no mortality (0/4) in rabbits exposed to 200, 632 and 2000 mg/kg. Scattered pathological findings included lung hemorrhage, kidney discoloration, pitted kidneys and peritoneal fluid accumulation.

L

Dermal irritation is of low concern based on slight erythema in rabbits exposed to 632 and 2000 mg/kg, and no irritation at 200 mg/kg.